ORIGINAL ARTICLE

LABETALOL VERSUS METHYLDOPA: EFFICACY IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Background: During pregnancy hypertension is an important medical problem and a major cause of maternal mortality. This study was designed to compare the efficacy of α and β-blocker labetalol and centrally acting methyldopa in controlling blood pressure in pregnancy induced hypertension.

Material & Methods: This study was carried out from June 2012 to May 2014 at Dow University Hospital OJHA Campus Karachi .A total of 120 patients having pregnancy induced hypertension were taken and divided randomly in to two groups. Group A was given labetalol 100mg tid and group B methyldopa 250 mg tid. In both the groups pre and post treatment systolic/diastolic BP was measured on day 1st and 7th and was compared. Following observations were made, reduction in BP, dose of drugs required to control BP, side effects of labetalol and methyldopa.

Results: Labetalol treated group of patients showed significant fall in systolic/diastolic BP from day 1st to 7th. In both the group pre and post treatment systolic/diastolic BP was measured and compared on first and 7th day. In patients treated with labetalol systolic/diastolic BP on 1st day was 150 $\pm$ 9 mmHg/100 $\pm$ 8 mmHg respectively and was controlled to 123 $\pm$ 9 mmHg/79 $\pm$ 7 mmHg on day 7, while systolic/diastolic BP in methyldopa treated group on 1st day was 148 $\pm$ 8 mmHg/102 $\pm$ 9 mmHg which was reduced to 125 $\pm$ 10 mmHg/82 $\pm$ 6 mmHg on day 7.

Conclusion: Labetalol indicated better antihypertensive action with less maternal and fetal side effects than methyldopa treated group and proved to be drug of choice in pregnancy induced hypertension.

KEY WORDS: Antihypertensive; Labetalol; Methyldopa; Pregnancy-induced hypertension.

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INTRODUCTION

No doubt health services have consistently been improved due to which maternal mortality rate is now efficiently controlled but still a large population of Pakistan is deprived of such progress and development in the field of health especially in case of female health. The analysis of maternal deaths due to various etiology shows that many causes of such deaths are quite preventable. About 10% pregnancies become very complicated due to hypertension resulting in maternal and fetal morbidity and mortality.[1]

During the first few weeks, the blood pressure of the pregnant woman's falls mainly due to blood vessels muscles relaxation but in the middle of the pregnancy it rises slowly to the normal blood pressure. The factors which can alter the blood pressure in pregnancy are physical activity, different position, time of the day, anxiety, diet, sleeping habits etc. Rise in blood pressure during pregnancy can cause serious complication like pre-eclampisia [1] which may results in failure of kidneys, liver, stroke, still birth, death of baby and many abnormalities of clotting system.[2]

If a women develops high BP after 20 weeks of pregnancy but don't have protein in her urine or other key symptoms of preeclampsia then she will be diagnosed with gestational hypertension, sometimes called pregnancy-induced hypertension (PIH). High blood pressure is addressed as big medical problem in pregnancy world wide it is an estimation that 6-8% pregnancies are complicated by hypertension.[3] Pre-eclampsia and eclampisia cause death in pregnant women in every 3 minutes throughout the world.[4,5] Labetalol and methyldopa have proved to be effective and safe for use in the

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pregnant women to control various hypertensive disorders during pregnancy.[6-10] High blood pressure causes complications in 10 percent of pregnancies [11] while progression from mild to severe forms of hypertension in pregnancy is impulsive and may be swift.[12] The use of anti-hypertensive medicines during pregnancy is controversial. The drug therapy has little place in the management of mild hypertension occurring late in the third trimester. It is observed that perinatal death has been shown to be lower in mild pregnancy induced hypertension .[13]but in moderate to severe hypertension with proteinuria, death rates are raised and active treatment results in a lower perinatal death rate.[13] In many ways management of pregnancy induced hypertension different from that of hypertension in non-pregnant individuals , with treatment generally being needed for a limited duration and at higher blood pressure targets in pregnancy induced hypertension. More over management of pregnancy induced hypertension mostly involves adjustment between challenging concerns for maternal health, gestational age of the infant and fetal exposure to antihypertensive drugs. The major goal of antihypertensive medication in pregnancy induced hypertension is to prevent or treat severe hypertension.

Pregnancy induced hypertension which is also called as gestational hypertension is normally treated with available oral medication but physicians have always many other challenges to deal with during pregnancy in case of high blood pressure. In order to save mother and fetus from the side effects of high blood pressure, many drugs are used to keep the blood pressure normal.[14] Severe hypertension causes severe maternal complications and to avoid these complication antihypertensive drugs are used.[15] Hypertension in pregnancy is treated with nifedipine, labetalol,hydralazine and methyldopa which are given orally.[16] This study was designed to evaluate and compare the efficacy of labetalol and methyldopa in the control of BP of patients with pregnancy induced hypertension.

MATERIAL AND METHODS

After taking written informed consent, 120 inpatients of Dow University Hospital OJHA Campus Karachi were enrolled in the present study and were divided randomly into two groups, A & B. Group A was treated with labetalol and group B was given methyldopa. Group A was given 100mg labetalol tid while group B had received 250mg tid methyldopa. In both the groups pre and post treatment systolic/ diastolic BP was measured. BP of patients in both the groups was monitored on 1st and 7th day. A comparison of labetalol and methyldopa was done on the basis of pre and post treatment recorded systolic/ diastolic BP. Following parameters were checked as regards of fall in BP with labetalol and methyldopa, time taken (days) by both to control BP, dose of both drugs required to control BP, onset of labor spontaneous/ induced, various side effects of both the drugs.

RESULTS

This study was carried out from June 2012 to May 2014 at Dow University Hospital OJHA Campus Karachi. All the confirm cases of pregnancy induced hypertension were included in the present study and the total number of inpatients were taken as sample which were 120, out of which 62 patients (51.66%) were in age group of 18-25 years, 33 patients (53.23%) were in group “A” and 29 patients (46.77 %) in group “B” while mean age of patients in group “A” and “B” was 25.64 years and 25.19 respectively. Statistically the mean age was non-significant in both the groups.

Present study shows that 76 patients were

Table 1: Systolic BP pre and post treatment value of day 1st and 7th in group A (Labetalol) and group B (Methyldopa).

S/No	Group	Numbers of patients	Pre Treatment value of systolic BP mmHg	Post treatment vale of systolic BP (mmHg)	t-value
1	Labetalol	60	150 ± 9	123 ± 9	11.21
2	Methyldopa	60	148 ±8	125 ± 10	14.02

Table 2: Diastolic BP pre and post treatment value of day 1st and 7th in group A (Labetalol) and group B (Methyldopa).

S/No	Group	Numbers of patients	Pre Treatment value of diastolic BP mmHg	Post treatment vale of diastolic BP (mmHg)	t-value
1	Labetalol	60	100 ± 8	79 ±7	11.81
2	Methyldopa	60	102 ± 9	82 ± 6	15.63

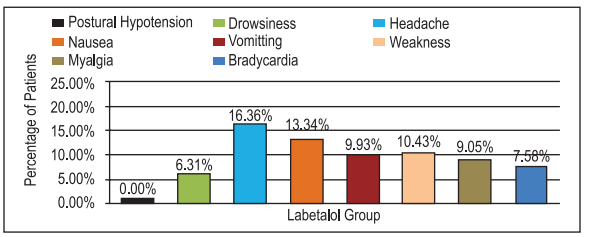

Figure 1: Distribution of patients according to side effect of labetalol.

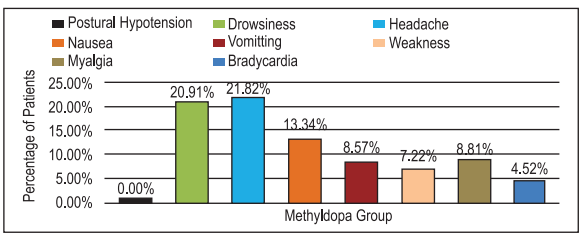

Figure 2: Distribution of patients according to side effect of methyldopa.

pregnant for the first time, 41 patients (53.94%) in methyldopa group and 35 patients (46.06%) in labetalol group. It is statistically non-significant difference between the two groups.

In both the group pre and post treatment systolic/diastolic BP was measured and compared on first and 7th day. In patients treated with labetalol systolic/diastolic on admission (1st day) was 150 ± 9 mmHg/100 ± 8 mmHg respectively and was controlled to 123 ± 9 mmHg/79 ± 7 mmHg on day 7th while systolic/diastolic BP in methyldopa treated group on the day of admission (1st day) was 148 ± 8 mmHg/102 ± 9 mmHg which was reduced to 125 ± 10 mmHg/82 ± 6 mmHg. Statistically significant reduction in systolic/diastolic BP was observed in case of labetalol treated group (Table 1,2)

Labetalol controls systolic/diastolic BP from 150 ± 9mmHg/100 ± 8 mmHg to 123 ± 9mmHg/79 ± 7 mmHg in 7 days while methyldopa has controlled systolic/diastolic BP from 148 ± 8 mmHg/102 ± 9 mmHg to 125 ± 10 mmHg/82 ± 6 mmHg in 7 days. Labetalol has reduced blood pressure relatively more as compare to methyldopa. This difference between the two is statistically significant.

In labetalol treated group 29 patients (48.33%) had spontaneous labor and 31 patients (51.66%) were induced while in methyldopa treated group 19 patients (31.66%) had spontaneous labor where as 41 patients (68.33%) had induced labor. These values were statistically significant $p<0.05$. In group A treated with labetalol, there were more numbers of patients having spontaneous labor indicating the fact that labetalol has ripening effect on the cervix.

The most common side effects found in both the groups where nausea, vomiting, myalgia, headache, weakness, drowsiness, bradycardia . There were 18 patients of headache in group A and 24 patients in group B. Patients felt more weakness treated with labetalol. Drowsiness was prominent side effect in methyldopa group. The total details of side effects of both the drugs are shown in Fig 1, 2.

DISCUSSION

There were 120 patients in total in this study, 60 patients in each group while in both the cases the numbers of patients with pregnancy induced hypertension were more in age group of 18-25 years. Pregnancy distribution indicates that there were greater numbers of women having pregnancy for the first time. The systolic/diastolic BP in labetalol group was 150 ± 9mmHg/100 ± 8mmHg on the day of admission which was reduced to 123 ± 9mmHg/79 ± 7 mmHg on day 7. It was statistically significant ($p<0.05$). In methyldopa treated group systolic/diastolic BP was 148 ± 8 mmHg/102 ± 9mmHg on day one which was controlled to 125 ± 10mmHg/82 ± 6 mmHg on 7th day. It is very clear comparison between the efficacy of labetalol and methyldopa that systolic/diastolic BP was comparable on day one but on day 7, the result of labetalol control (123 ± 9mmHg/79 ± 7 mmHg) was better than methyldopa (125 ± 10 mmHg/82 ± 6 mmHg). Our study shows that systolic/diastolic BP was somewhat same in both the group before treatment but significant fall in systolic/diastolic BP is observed on day 7 in group treated with labetalol which is in accordance with the study done by lamming.[17] Another study indicates that fall in systolic/diastolic BP was significant with labetalol than methyldopa treated group.[18] In the same study 81.4% patients receiving labetalol had significant fall in systolic/diastolic BP as compare to methyldopa treated group which were 68.5% patients. In our study labetalol shows control on systolic/diastolic BP more as compare to methyldopa which could control systolic/diastolic BP less than laetalol. Labetalol has controlled BP significantly more than methyldopa. It is in accordance with the study in which it was shown that 45 (88%) patients out of 51 patients had shown rapid control of BP receiving oral labetalol.[18] Many other studies support our result including the studies of lardoux's,[17] 82% and, Michal[18] 92 %. Results of our study are in accordance with other studies which show that minimum incidence of maternal and foetal side effects with very good perinatal outcomes confirm the suitability of labetalol for its use in pregnancy induced hypertension instead of methyldopa[17] as is stated in another study that α and β blocker labetalol has batter control of BP.[18]

CONCLUSION

Labetalol indicated better antihypertensive action with less maternal and fetal side effects than methyldopa treated group and proved to be drug of

choice in pregnancy induced hypertension.

REFERENCES

1. Roberts JM, Redman CWG. Pre-eclampsia: more than pregnancy-induced hypertension. Lancet 1993; 341:1447–51.
2. Redman CWG, Roberts JM. Management of pre-eclampsia. Lancet 1993; 341:1451–4.
3. Magee LA, Ornstein MP, Dadelszen P. Fortnightly review: management of hypertension in pregnancy. BMJ 1999; 318:1332-6.
4. Giannubilo SR, Bezzeccheri V, Cecchi S, Landi B, Battistoni GI, Vitali P, et al. Nifedipine versus labetalol in the treatment of hypertensive disorders of pregnancy. Arch Gynecol Obstet 2012; 286:637-42.
5. Khedun SM, Moodley J, Naicker T. Drug management of hypertensive disorders of pregnancy. Pharmacol Ther 1997; 74:221-58.
6. Mabie WC. Management of acute severe hypertension and encephalopathy. Clin Obstet Gynecol 1999; 42:519-31.
7. Linton DM, Anthony J. Critical care management of severe pre-eclampsia. Intensive Care Med 1997; 23:248-55.
8. Lenfant C. National Education Program Working Group on High Blood Pressure in Pregnancy. Working group report on high blood pressure in pregnancy. J Clin Hypertens 2001; 3:75-88.
9. Sibai BM. Eclampsia. VI. Maternal-perinatal outcome in 254 consecutive cases. Am J Obstet Gynecol 1990; 163:1049-54.
10. Leather HM, Humphreys DM, Baker P, Chadd MA. A controlled trial of hypotensive agents in hypertension in pregnancy. Lancet 1968; 2:488-90.
11. Podymow T, August P. Update on the use of antihypertensive drugs in pregnancy. Hypertension 2008; 51:960-9.
12. Brown MA, Hague WM, Higgins J. The detection, investigation and management of hypertension in pregnancy: executive summary. Consensus statement from the Australasian Society for the Study of Hypertension in Pregnancy. Aust N Z J Obstet Gynaecol 2000; 40:133-8.
13. Lamming GD, Symonds EM. Use of Labetalol and Methyldopa in Pregnancy-Induced Hypertension. Br J Clin Pharmacol. 1979; 8:217S-222S.
14. El-Qarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. Labetalol vs. methyldopa in the treatment of pregnancy-induced hypertension. Int J Gynaecol Obstet 1995; 49:125-30.
15. Cruickshank DJ, Robertson AA, Campbell DM, MacGillivray I. Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Eur J Obstet Gynecol Reprod Biol 1992; 45:47-51.
16. Lardoux H, Gerard J, Blazquez G, Chouty F, Flouvat B. Hypertension in pregnancy: evaluation of the two β-blockers atenalol and labetalol. Eur Heart J 1983; 4:35-40.
17. Michael CA. Use of labetalol in the treatment of severe hypertension during pregnancy. Br J Clin Pharmacol 1979; 8:211S-215S.
18. Michael CA.The evaluation of labetalol in the treatment of hypertension complicating pregnancy. Br J Clin Pharmacol 1982; 13:127S-131S.

CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.